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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,950	03/19/2004	Christine Konradi	04843/120003	8080

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CLARK & ELBING LLP
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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,950	KONRADI ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *3-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed 12/04/2006. Currently Claims 1-39 are pending. Claims 3-38 have been withdrawn as being drawn to a nonelected invention.

2. A complete reply to the final rejection must include cancellation of nonelected claims and subject matter or other appropriate action (37 CFR 1.144) See MPEP § 821.01. As stated in the response to the restriction filed 4/20/2006, applicant has elected without traverse a specific set of genes: ATP synthase, F1 complex, O subunit; ATP synthase, F0 complex, d subunit; ATP synthase, F0 complex, c3 subunit; ATP synthase, F1 complex, gamma polypeptide 1; and ATP synthase, F0 complex, subunit F. Applicant should amend the claims so that the claims are directed to the elected invention of the specific combination of genes.

3. The following rejections to Claims 1-2 and 39 are applied as necessitated by amendment or are reiterated. Response to arguments follows.

4. This action is FINAL.

Withdrawn Objections

5. The objection to the specification made in section 4 of the previous office action has been withdrawn based on amendments to the specification.

Withdrawn Rejections

6. The rejection of Claims 1-2 under 35 USC 102(b) in section 8 of the previous office action has been withdrawn based on amendments to the claims.

7. The rejection of Claims 1-2 under 35 USC 102(e) in section 9 of the previous office action has been withdrawn based on amendments to the claims.

Reiterated Rejections and Rejections Necessitated by amendment

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1- 2 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claim 1 is drawn to a microarray of mitochondrial energy metabolism nucleic acid molecules. Claim 2 is drawn to a microarray consisting of ATP synthase, F1 complex, O subunit; ATP synthase, F0 complex, d subunit; ATP synthase, F0 complex, c3 subunit; ATP synthase, F1 complex, gamma polypeptide 1; and ATP synthase, F0 complex, subunit F. Claim 39 is drawn to the microarray of claim 1 wherein the microarray comprises fragments of at least 40 nucleotides.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Guidance in the Specification and Working Examples

The specification teaches microarrays comprising at least 2, 5, 10, 15, 20, 30, 40, 50, or 60 nuclear encoded mitochondrial energy metabolism nucleic acid molecules, or fragments thereof, bound to a solid support, where at least 90%, 95%, or 100% of the nucleic acid molecules on the support are nuclear encoded mitochondrial energy metabolism nucleic acid molecules (p. 2). The specification does not describe by sequence identification which parts of the mitochondrial energy metabolism nucleic acid molecules are placed on the array, therefore it is unpredictable what actual sequences are placed on the array. It is unclear which parts of the gene was known at the time of

the invention because the only descriptive information is Genbank numbers which by themselves do not define a sequence because the sequences provided by Genbank numbers can be altered.

The specification defines "nuclear encoded mitochondrial energy metabolism nucleic acid molecule" as a polynucleotide or fragment that occurs in the nucleus and encodes a polypeptide that localizes to the mitochondria or functions in mitochondrial energy metabolism (p. 18). The specification teaches a nucleic acid microarray is composed of oligonucleotides having at least a portion of two or more nucleic acid sequences listed in Table 2 (p. 18). The specification teaches a "portion" of a fragment of a nucleic acid that is substantially identical to a reference nucleic acid (p. 19). The specification portion retains at least 50%, 75%, 80%, 90%, 95%, or even 99% of the biological activity of the referent nucleic acid (p. 19). Table 3 provides the function of the gene products encoded by these down regulated genes, their subcellular localization, and Genepept sequence identifiers (p. 30).

The specification fails to define what is encompassed by nuclear encoded mitochondrial energy metabolism nucleic acid molecule because the specification does not describe any genes in a way in which the ordinary artisan would know which portions of the referent nucleic acid retains a specific portion of biological activity. It is unpredictable as to which parts of a sequence should be on the array since the specification provides not details as to which portions of the sequence retain the specific mitochondrial energy metabolism activity. It is unpredictable as to the actual sequences

encompassed on the array because the specification only defines the sequences based on Genbank accession numbers which are not static and can be updated.

Therefore the ordinary artisan would have to do undue experimentation in order to determine which sequences are encompassed by the array. The ordinary artisan would have to determine which parts of the sequence would provide the necessary retention in activity in order to distinguish a sequence as a specific mitochondrial energy metabolism activity nucleic acid. Further the ordinary artisan is not provided with any defining characteristics of the sequences on the array except Genbank accession numbers. The ordinary artisan would have to perform undue experimentation to determine which parts of sequences should be used from a Genbank accession number that can continually be updated.

The unpredictability of the art and the state of the prior art

The state of the art teaches that there are updates to Genbank accession numbers and therefore to define a sequence solely on an accession number encompasses a large genus of potential sequence changes which is not known at the time of filing. For example, Accession No. AF047436 was submitted on 2/10/1998, but the sequence had an update to its sequence on 11/21/2002. It is unpredictable based on just the Genbank accession number which sequence was used to create the array. It is undefined if the sequence used was the original sequence submitted or the most recently updated. It is unclear which parts of the sequence has been changed and the effect of the changes.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters that would have to be studied. To practice the

invention as broadly as it is claimed, the skilled artisan would be required to produce an array without knowing which parts of the listed sequences would retain functionality. The skilled artisan would also be required to produce an array from sequences that are updated so therefore it is unpredictable if the array built by sequences on one date would be the same array built on another date. It is unclear what actual sequences the specification was in possession of at the date of filing because there is no description of the sequence provided that is not changeable.

The skilled artisan would need to perform undue experimentation to determine which parts of the sequences would be used on the array and the actual sequence of the gene on the array since the nucleic acids are defined with Accession numbers which can be updated.

To use the invention as presented would require a large amount of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus the applicants have not provided sufficient guidance to enable a skilled artisan to make the claimed invention in a manner reasonably correlated with the genus of the claims because the genus of the claims include nucleic acid sequences that can be updated and include sequences with any number of nucleic acids. The sequences on the arrays are not defined by the specific number of nucleic acids which the sequence needs to have in order to be defined as a "functional" nuclear encoded mitochondrial energy metabolism nucleic acid molecule. Without sufficient guidance, it is unpredictable and the experimentation left to those skilled in the art is extensive.

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, and the lack of guidance provided in the specification balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The reply traverses the rejection. (A) The reply asserts that the GenBank accession number specifically and uniquely identifies a sequence (p. 19). The reply asserts that the skilled artisan can determine if a sequence has been changed from the original submission (p. 19). The reply asserts that of the four versions of AF047436 searched in NCBI all contained the same sequence (p. 20 end of 1st paragraph). The reply asserts that a GenBank number provides reference to a specific sequence and the GenBank database tracks the changes associated with an assession number (p. 20 last paragraph). (B) The reply asserts even if there are changes in the GenBank sequences one skill in the art could still practice the invention (p. 21 1st paragraph). The reply assets that the nucleotides used are to form microarrays in which an exact sequence match is not required for hybridization to take place (p. 21 1st paragraph). (C) The reply asserts that the there has been no demonstration that potential changes represent a practical issue for making or using the claimed invention (p. 21 last paragraph). The reply asserts that none of the 5 GenBank assession numbers of the claimed genes has undergone a sequence revision since filing of the application and that there is no evidence for the potential for such changes (p. 22 1st paragraph). (D) The reply asserts that the identification of a gene with a known sequence by name is sufficient to identify

the sequence associated with that gene (p. 22 last paragraph). The reply asserts that Falkner v. Inglis support that determining a known sequence form the name of a gene would not require undue experimentation (p. 22 last paragraph). (E) The reply asserts that the nucleic acids on the claimed array do not need to encode functional proteins, but they need only to provide sequences to which other nucleic acids hybridize (p. 23 1st full paragraph). The reply asserts that the nucleic acids on the array hybridize to mRNAs that include the entire coding sequence of mitochondrial metabolism genes the nucleic acids of the array need not encode any particular fragment except a hybridizable element (p. 23 1st full paragraph). The reply asserts that a nucleic acid can be used in the array if it can hybridize to the appropriate test nucleic acid (p. 23 last paragraph).

These arguments have been thoroughly reviewed but have not been found persuasive.

(A) Though the skilled artisan can determine if a sequence has been changed from the original submission in GenBank, the disclosure is not enabling because the nucleic acid sequences that are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

MPEP 608.01(p)[R-2] states that "While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention.

By referring to the GenBank Accession Number, the claims seek to incorporate by reference the subject matter of the sequences set forth in the recited GenBank records. This constitutes an improper incorporation by reference to essential subject matter since this subject matter is necessary to describe the claimed invention.

Essential material may not be incorporated by reference to non-patent publications (see MPEP 608.01(p)). Therefore, the claims are rejected for failure to comply with the enablement requirement because the specification fails to provide essential subject matter for the practice of the claimed invention.

The skilled artisan could track changes in an accession number sequence, however, GenBank accession numbers sequences and accompany text are continuously updated and modified. Therefore, there is no single, fixed definition for the sequence presented as GenBank Accession NO. Therefore, the skilled artisan would not know which variants, fragments, or homologs of the sequence would be encompassed by the gene name.

(B) Though, the changes are trackable, the use of a GenBank accession number as a sequence of a particular gene is insufficient. GenBank accession numbers sequences and accompany text are continuously updated and modified, therefore, there is no single, fixed definition for the sequence presented as GenBank Accession number. The skilled artisan would not know which version of the sequence could be used on the array. Further, the skilled artisan would have to perform undue experimentation in order to determine if any fragment of the changed sequence would produce the same results.

(C) The reply asserts that there is no demonstration that potential changes represent a practical issue for making or using the claimed invention. It is well known in the art, however, that a change to a sequence affects the ability of that sequence to hybridize. Therefore, it is unclear if ANY fragments of the particular genes claimed which would include any number of mutations and homolog would be able to produce

the same array. Further, as addressed above, the GenBank accession number does not provide a clear static definition of the gene names claimed.

(D) The response cites Falko-Gunter Falkner vs. Inglis, 448 F.3rd, 1357, Federal Circuit as stating that sequence information is not required to be present in the specification. However, the facts of this case are clearly distinct from those herein. In the cited case, it was determined that it was sufficient to refer to a gene only by the gene name since the gene was well known in the art and the particular nucleotide sequence of the gene was not critical to the claimed invention. In contrast, in the present situation, the claims are drawn to fragments of specific genes. Each fragment of the gene would give a different expression pattern and therefore a different association with a phenotypic response (in the instant case bipolar disorder). Therefore the particular sequence of the gene is critical for the invention. Therefore, the two cases differ in the fact that in the Flakner case the sequence of the gene did not effect the invention, however, in the present case, the sequence would effect the invention because different sequences will produce different expression patterns.

(E) The nucleic acids do not need to encode functional proteins, however, the disclosure is not enabled because the claims encompass a large number of nucleic acid fragments. The skilled artisan would have to perform undue experimentation in order to determine which fragments placed on a array will be functionally equivalent. The function of the array is not the ability to be hybridizable but the ability to produce an expression level correlated with bipolar disorder. Any fragment of the genes listed including fragments of mutations, variants, and homologs would not be functionally the

same. Further, the claims are not drawn to nucleic acids, which hybridize to mRNAs that include the entire coning sequence of mitochondrial metabolism genes. The claims are drawn to any fragment of nucleic acids of 15 mer or 40 mer nucleotides of the elected genes. Because the specification does not disclose which nucleotides are required to be considered a particular gene, the claims broadly encompass a large number of variants, mutants, and homologs. These fragments are not disclosed in the specification in a way in which the skilled artisan could readily determine their functionality without undue experimentation.

Claim Rejections - 35 USC § 112-Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1- 2 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an isolated nucleic acid molecule comprising the sequence of SEQ ID No. 1. Claim 2 is drawn to an isolated nucleic acid molecule comprising a sequence

complementary to the sequence of SEQ ID No. 1. Claim 39 is drawn to the microarray of claim 1 wherein the microarray comprises fragments of at least 40 nucleotides.

The claims do not describe the number or identity of nucleotides needed to be considered a nuclear encoded mitochondrial energy metabolism nucleic acid. The claims encompass nucleic acids defined by Genbank accession numbers which can be update and would therefore comprise any nucleic acid variant of any size of at least 15 mer or at least 40 mer, fragments of the sequences presented. The claims would encompass updates to the Genbank accession numbers could have variants, which include nucleotide substitutions, additions, deletions, translocations, and truncations. The specification does not describe the sequences encompassed by "nuclear encoded mitochondrial energy metabolism nucleic acid"

The claims also encompass a large genus of sequences of any size of at least 15 mer or at least 40 mer with no defining characteristics to nuclear encoded mitochondrial energy metabolism nucleic acid. An array of sequences could all be 15 mer in length and be considered as have at least 90% of the nucleic acids as nuclear encoded mitochondrial energy metabolism nucleic acid but the 15 mer nucleic acids could be any number of potential sequences.

The specification fails to describe the sequences of the mitochondrial energy metabolism nucleic acid molecules based on size. The specification depends on the description of a Genbank accession number to define the nucleic acids encompassed by the claims, but since accession numbers can be updated the specification fails to provide fixed sequences and therefore the claims include any number of possible variants.

The specification teaches that the array must include some fragment of ATP synthase, F0 complex, subunit F and point in the specification to Genbank Accession

AF047436. It is unclear, though, based solely on an accession number what constitutes an ATP synthase, F0 complex, subunit F genes sequence. Accession AF047436 has been updated since its initial submission. It is unclear which sequence, the initial or the updated, should be on the array. The specification fails to describe which nucleic acids should be placed on the array and the size of the nucleic acid sequences.

The genus of the claimed nucleic acids molecules encompasses substantial variability among the species of nucleic acids because the accession numbers, which can have enumerable updates, are the only defining characteristic of the nucleic acid molecules. The genus of the claimed invention encompasses a large variable genus of mutants, variants, and homologs from any source. The specification fails to sufficiently describe the claimed invention in clear and exact terms so that a skilled artisan would recognize that the applicants were in possession of the claimed invention at the time of filing.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids in view of the species

disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The sequences encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes

clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

The reply traverses the rejection. (A) The reply asserts changes to sequence in the GenBank database are trackable (p. 24 last sentence). The reply asserts that the claims have been amended to a particular length (p. 25 last paragraph). (B) The reply asserts that the specification providers both structure and function to the genus of nucleic acids encompassed by the claims (p. 26 1st paragraph). The reply asserts that the structure is nuclear encoded mitochondrial energy metabolism nucleic acids and the function is the ability to hybridize when used in an array (p. 26). The reply asserts that there is a body of literature describing nuclear encoded mitochondrial energy metabolism genes and therefore it is not necessary to include sequence to genes known in the art (p. 26 1st paragraph). The reply points to Flakner v. Inglis (p. 26). The reply asserts that as for function the nucleic acids used in an array must have the ability to hybridize to mRNA encoding a mitochondrial energy metabolism gene and that the phrase "hybridizable array elements" reflect the function (p. 27 1st paragraph).

These responses have been fully considered but have not been found persuasive.

(A) As discussed above in the response to the 112/Enablement rejection by referring to the GenBank Accession Number, the claims seek to incorporate by reference the subject matter of the sequences set forth in the recited GenBank records.

This constitutes an improper incorporation by reference to essential subject matter since this subject matter is necessary to describe the claimed invention. Essential material may not be incorporated by reference to non-patent publications (see MPEP 608.01(p)). Therefore, the claims are rejected for failure to comply with the enablement requirement because the specification fails to provide essential subject matter for the practice of the claimed invention.

Further even though the claims have been amended to a particular sequence length, the claims still encompass a very large genus of nucleic acid fragments. The specification has not describe the genus of nucleic acid fragments in such a way such that the skilled artisan would be able to determine the nucleotides which are encompassed by the broad claim language.

(B) The response cites Falko-Gunter Falkner vs. Inglis, 448 F.3rd, 1357, Federal Circuit as stating that sequence information is not required to be present in the specification to describe the invention. However, the facts of this case are clearly distinct from those herein. In the cited case, it was determined that it was sufficient to refer to a gene only by the gene name since the gene was well known in the art and the particular nucleotide sequence of the gene was not critical to the claimed invention. In contrast, in the present situation, the claims are drawn to fragments of specific genes. Each fragment of the gene would give a different expression pattern and therefore a different association with a phenotypic response (in the instant case bipolar disorder). Therefore the particular sequence of the gene is critical for the invention. Therefore, the two cases differ in the fact that in the Flakner case the sequence of the gene did not

effect the invention, however, in the present case, the sequence would effect the invention because different sequences will produce different expression patterns. The claims encompass a large number of nucleic acid fragments including mutants, variants, and homologs of the claimed genes. The specification has not adequately described this genus of nucleic acids therefore the claims encompass a large number of sequences without any guidance in the specification as to which sequences would be considered a functional equivalent of the claimed genes.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Affymetrix Human Genome U95A array (Affymetrix Product Catalog January 2001) and by the Affymetrix Website (www.affymetrix.com).

With regard to Claims 1-2, the Affymetrix U95A Gene Chip discloses: probe 34811_at (GenBank Accession No. U09813); probe 35760_at (GenBank Accession No. AF087135); probe 40134_at (GenBank Accession No. AF047436); probe

37029_at (GenBank Accession No. X83218); and probe 40115_at (GenBank Accession No. D16562). These probes are from the same GenBank numbers as the genes listed in Table 3 for the genes of Claims 1 and 2. Therefore the Affymetrix U95 gene chip encompasses all the limitations of the claims.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Katherine Salmon
Examiner
Art Unit 1634

CARLA J. MYERS
PRIMARY EXAMINER